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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

HOSPIRA, INC. and ORION CORPORATION, Plaintiffs, v. SANDOZ INTERNATIONAL GmbH, SANDOZ INC., and SANDOZ CANADA INC. Defendants.	Civil Action No. 3:09-cv-04591-MLC-TJB Filing Date: September 4, 2009 Judge Mary L. Cooper **REDACTED VERSION**
SANDOZ INC. Counterclaim-Plaintiff, v. HOSPIRA, INC. and ORION CORPORATION, Counterclaim-Defendants.	

SANDOZ CANADA INC.'S FIRST AMENDED ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' AMENDED COMPLAINT

Defendant Sandoz Canada ("Sandoz Canada"), by and through its undersigned attorneys, hereby answers each of the numbered paragraphs of the Amended Complaint filed on May 17, 2010, by Hospira, Inc. ("Hospira") and Orion Corp. ("Orion") (collectively "Plaintiffs"). Except

as expressly admitted below, Sandoz Canada denies each allegation of the Plaintiffs' Amended Complaint.

PARTIES

1. Sandoz Canada admits the allegations of Paragraph 1.

2. Sandoz Canada admits that Orion is a corporation with its principal place of business at Orionintie 1A, FI-02200 Espoo, Finland. Sandoz Canada lacks knowledge or information sufficient to form a belief as to the truth of the remaining allegations in Paragraph 2 and therefore denies them.

3. Sandoz Canada admits that Sandoz International GmbH is a German corporation. Sandoz Canada denies that Sandoz International GmbH has a principal place of business at Industriestrasse 25, Holzkirchen 83607, Germany.

4. Sandoz Canada lacks knowledge or information sufficient to form a belief as to the truth of the allegations of Paragraph 4 and therefore denies them.

5. Sandoz Canada admits the allegations of Paragraph 5.

6. Sandoz Canada denies the allegations of Paragraph 6.

7. Sandoz Canada denies the allegations of Paragraph 7.

8. Sandoz Canada denies the allegations of Paragraph 8.

9. Sandoz Canada denies the allegations of Paragraph 9.

10. The allegations in Paragraph 10 are directed to another Defendant and therefore require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required, Sandoz Canada objects that the allegations in Paragraph 10 are not "simple, concise, and direct" as required under Federal Rule of Civil Procedure 8(d)(1) and, on that basis,

denies the allegations of Paragraph 10. To the extent that a response is nevertheless required despite Sandoz Canada's objection, Sandoz Canada denies the allegations of Paragraph 10.

11. Sandoz Canada denies the allegations of Paragraph 11.

12. Sandoz Canada admits that it manufactures certain generic pharmaceutical products, and denies the remaining allegations of Paragraph 12 directed to Sandoz Canada. To the extent that the allegations in Paragraph 12 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required despite Sandoz Canada's objection, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

13. Sandoz Canada denies the allegations of Paragraph 13.

14. The allegations in Paragraph 14 are directed to another Defendant and therefore require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required, Sandoz Canada objects that the allegations in Paragraph 14 are not "simple, concise, and direct" as required under Federal Rule of Civil Procedure 8(d)(1) and, on that basis, denies the allegations of Paragraph 14. To the extent that a response is nevertheless required despite Sandoz Canada's objection, [REDACTED].

NATURE OF THE ACTION

15. Sandoz Canada admits that this is a civil action involving U.S. Patent Nos. 4,910,214 ("the '214 patent") and 6,716,867 ("the '867 patent").

16. As to the allegations against Sandoz Canada, Sandoz Canada admits that this action is based upon the United States patent laws, 35 U.S.C. § 1 *et seq*., and that this action relates to an Abbreviated New Drug Application ("ANDA") seeking approval to sell

Dexmedetomidine Hydrochloride Injection 100 mcg base/ml prior to the expiration of the '214 and '867 patents, which are listed in the Orange Book in connection with the proprietary name PRECEDEX. Sandoz Canada denies the remaining allegations of Paragraph 16 directed to Sandoz Canada. To the extent that allegations in Paragraph 16 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required despite Sandoz Canada's objection, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

JURISDICTION AND VENUE

17. Sandoz Canada admits the allegation of Paragraph 17.

18. Sandoz Canada admits the allegation of Paragraph 18.

19. The allegations in Paragraph 19 are directed to another Defendant and therefore require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

20. The allegations in Paragraph 20 are directed to another Defendant and therefore require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

21. Sandoz Canada denies the allegations of Paragraph 21.

22. Sandoz Canada denies that venue is proper in this District.

THE PATENTS-IN-SUIT

23. Sandoz Canada admits that the '214 patent is entitled "Optical Isomer of an Imidazole Derivative Medetomidine as an Alpha-2-Receptor Agonist" and issued on March 20, 1990. Sandoz Canada denies that the '214 patent was duly and legally issued by the United States Patent and Trademark Office ("PTO"). Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations in Paragraph 23 and therefore denies them.

24. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations in Paragraph 24 and therefore denies them.

25. Sandoz Canada admits that the '867 patent is entitled "Use of Dexmedetomidine for ICU Sedation" and issued on April 6, 2004. Sandoz Canada denies that the '867 patent was duly and legally issued by the PTO. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations in Paragraph 25 and therefore denies them.

26. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations in Paragraph 26 and therefore denies them.

27. Sandoz Canada admits that New Drug Application No. 021038 was approved on December 17, 1999, and lists Hospira as the Company, Dexmedetomidine as the Active Ingredient, 100 mcg base/mL as the Strength, injection as the Dosage Form, and PRECEDEX as the proprietary Drug Name.

28. Sandoz Canada admits that the '214 and '867 patents are listed in the Orange Book in connection with the proprietary Drug Name PRECEDEX. Sandoz Canada denies that the claims of the '214 and/or '867 patents cover PRECEDEX or any formulations or methods of use thereof.

ACTS GIVING RISE TO THIS ACTION

29. Sandoz Canada denies the allegations of Paragraph 29 that are directed to Sandoz Canada, except admits that it reviewed certain information concerning Hospira's Precedex™ [REDACTED].. To the extent that the allegations in Paragraph 29 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required despite Sandoz Canada's objection, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

30. Sandoz Canada denies the allegations of Paragraph 30.

31. Sandoz Canada admits the allegations of Paragraph 31.

32. Sandoz Canada [REDACTED].

33. Sandoz Canada admits the allegations of Paragraph 33.

34. The allegations in Paragraph 33 are directed to another Defendant and therefore require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response is required, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

35. Sandoz Canada admits that it manufactures certain injectable pharmaceutical products.

36. Sandoz Canada [REDACTED] and otherwise denies the allegations of Paragraph 36.

37. Sandoz Canada admits that Sandoz Inc. has distributed and sold at least one generic pharmaceutical product for which Sandoz Canada has received FDA approval. Sandoz Canada otherwise denies the allegations of Paragraph 37.

38. Sandoz Canada [REDACTED]. Sandoz Canada otherwise lacks knowledge or information sufficient to form a belief about the truth of the remaining allegations of Paragraph 38 and therefore denies them.

39. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 39 and therefore denies them.

40. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 40 and therefore denies them.

41. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 41 and therefore denies them.

42. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 42 and therefore denies them.

43. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 43 and therefore denies them.

44. Sandoz Canada denies the allegations of Paragraph 44 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 44 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

45. Sandoz Canada admits that it was aware of the patents-in-suit when ANDA No. 91-465 containing a Paragraph IV certification was filed. To the extent that the allegations in Paragraph 45 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B).

46. Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of the allegations of Paragraph 43 and therefore denies them.

RESPONSE TO FIRST CLAIM FOR RELIEF

(Denial of Infringement of the '214 Patent)

47. Sandoz Canada admits that Plaintiffs incorporated Paragraphs 1 through 46 as previously set forth in the Amended Complaint, and incorporates its responses thereto.

48. Sandoz Canada [REDACTED] and otherwise denies the allegations of Paragraph 48.

49. Sandoz Canada denies the allegations of Paragraph 49 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 49 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

50. Sandoz Canada admits that it was aware of the '214 patent prior the filing of ANDA No. 91-465, and otherwise denies the allegations of Paragraph 50 directed to Sandoz Canada. To the extent that the allegations in Paragraph 50 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

51. Sandoz Canada denies the allegations of Paragraph 51.

RESPONSE TO SECOND CLAIM FOR RELIEF

(Denial of Infringement of the '867 Patent)

52. Sandoz Canada admits that Plaintiffs incorporated Paragraphs 1 through 51 as previously set forth in the Amended Complaint, and incorporates its responses thereto.

53. Sandoz Canada [REDACTED] and otherwise denies the allegations of Paragraph 53.

54. Sandoz Canada denies the allegations of Paragraph 54 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 54 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

55. Sandoz Canada denies the allegations of Paragraph 55 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 55 are directed to another Defendant, such allegations require no response from Sandoz. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

56. Sandoz Canada admits that it was aware of the '867 patent prior the filing of ANDA No. 91-465, and otherwise denies the allegations of Paragraph 56 directed to Sandoz Canada. To the extent that the allegations in Paragraph 56 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada lacks knowledge or information sufficient to form a belief about the truth of such allegations and therefore denies them.

57. Sandoz Canada denies the allegations of Paragraph 57 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 57 are directed to another Defendant,

such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

RESPONSE TO THIRD CLAIM FOR RELIEF

(Denial of Inducement of Infringement of the Patents-in-Suit)

58. Sandoz Canada admits that Plaintiffs incorporated Paragraphs 1 through 57 as previously set forth in the Amended Complaint, and incorporates its responses thereto.

59. Sandoz Canada denies the allegations of Paragraph 59 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 59 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

60. Sandoz Canada denies the allegations of Paragraph 60 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 60 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

61. Sandoz Canada denies the allegations of Paragraph 61 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 61 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

62. Sandoz Canada denies the allegations of Paragraph 62 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 62 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

63. Sandoz Canada denies the allegations of Paragraph 63 that are directed to Sandoz Canada. To the extent that the allegations in Paragraph 63 are directed to another Defendant, such allegations require no response from Sandoz Canada. *See* Fed. R. Civ. P. 8(b)(1)(B). To the extent that a response to allegations against another Defendant is required, Sandoz Canada denies such allegations.

AFFIRMATIVE DEFENSES

Without admitting or implying that Sandoz Canada bears the burden of proof as to any of them, Sandoz Canada asserts, on information and belief, the following affirmative defenses:

FIRST AFFIRMATIVE DEFENSE

(Failure to State a Claim)

1. The Amended Complaint fails to state a claim upon which relief can be granted.

SECOND AFFIRMATIVE DEFENSE

(Noninfringement of the '214 Patent)

2. Sandoz Canada has not infringed, induced infringement of, or contributed to the infringement of any valid and enforceable claim of the '214 patent.

THIRD AFFIRMATIVE DEFENSE

(Invalidity of the '214 Patent)

3. The '214 patent, and each claim thereof, is invalid for failing to comply with the requirements of the patent laws of the United States, particularly with regard to one or more of the requirements specified in Sections 101, 102, 103, and/or 112 of Title 35 of the United States Code.

FOURTH AFFIRMATIVE DEFENSE

(Inequitable Conduct During Prosecution of the '214 Patent)

4. The '214 patent is unenforceable as a result of inequitable conduct during prosecution before the PTO, as particularly explained and alleged in the Third Counterclaim.

FIFTH AFFIRMATIVE DEFENSE

(Noninfringement of the '867 Patent)

5. Sandoz Canada has not infringed, induced infringement of, or contributed to the infringement of any valid and enforceable claim of the '867 patent.

SIXTH AFFIRMATIVE DEFENSE

(Invalidity of the '867 Patent)

6. The '867 patent, and each claim thereof, is invalid for failing to comply with the requirements of the patent laws of the United States, particularly with regard to one or more of the requirements specified in Sections 101, 102, 103, and/or 112 of Title 35 of the United States Code.

SEVENTH AFFIRMATIVE DEFENSE

(Inequitable Conduct During Prosecution of the '867 Patent)

7. The '867 patent is unenforceable as a result of inequitable conduct during prosecution before the PTO, as particularly explained and alleged in the Sixth Counterclaim below.

EIGHTH AFFIRMATIVE DEFENSE

(Unclean Hands)

8. The patents-in-suit are unenforceable under the doctrine of unclean hands.

NINTH AFFIRMATIVE DEFENSE

(Lack of Personal Jurisdiction)

9. This Court lacks personal jurisdiction over Sandoz Canada.

TENTH AFFIRMATIVE DEFENSE

(Miscellaneous Reservation of Rights)

10. Sandoz Canada presently asserts the above defenses without the benefit of full discovery and investigation, and reserves the right to supplement or amend these affirmative defenses as necessary.

COUNTERCLAIMS

Defendant and Counterclaimant Sandoz Canada Inc. hereby submits these Counterclaims against Hospira and Orion ("Plaintiffs"):

JURISDICTION AND VENUE

1. The Court has subject matter jurisdiction over these Counterclaims under the provisions of 28 U.S.C. § 1331, 1338(a), and 1367(a).

2. Venue in this district is also proper pursuant to 28 U.S.C. § 1391(b) and (c) in that Plaintiffs are subject to the personal jurisdiction of this Court by commencing and continuing to prosecute this action; because a substantial part of the events giving rise to Sandoz Canada's counterclaims occurred in this district; and each Counterdefendant is found or transacts business in this judicial district.

3. Sandoz Canada asserts these counterclaims as compulsory, without admitting and expressly preserving its affirmative defenses, including its defense that Plaintiffs have failed to state a claim upon which relief can be granted and that this Court lacks personal jurisdiction over Sandoz Canada.

FIRST COUNTERCLAIM

(Declaratory Judgment of Noninfringement of the '214 Patent)

4. Sandoz Canada hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 63 of its Answer, 1 through 10 of its Affirmative Defenses, and 1 through 3 of these Counterclaims above.

5. Sandoz Canada and its Dexmedetomidine Hydrochloride Injection 100 mcg base/ml product (the "Sandoz product") do not infringe the '214 patent, directly or indirectly, either literally or by the doctrine of equivalents.

6. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding whether Sandoz Canada infringes the '214 patent, and a judicial declaration of noninfringement is necessary and appropriate at this time.

SECOND COUNTERCLAIM

(Declaratory Judgment of Invalidity of the '214 Patent)

7. Sandoz Canada hereby incorporates by reference each and every allegation set forth in Paragraphs 1 through 63 of the Answer, 1 through 10 of the Affirmative Defenses, and 1 through 6 of these Counterclaims above.

8. The '214 patent, and each claim thereof, is invalid for failing to comply with the requirements of the patent laws of the United States, particularly with regard to one or more of the requirements specified in Sections 101, 102, 103, and/or 112 of Title 35 of the United States Code.

9. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding the validity of the '214 patent, and a judicial declaration of invalidity is necessary and appropriate at this time.

THIRD COUNTERCLAIM

(Declaratory Judgment of Unenforceability of the '214 Patent)

10. Sandoz Canada hereby incorporates by reference each and every allegation set forth in Paragraphs 1 through 63 of the Answer, 1 through 10 of the Affirmative Defenses, and 1 through 8 of these Counterclaims above.

11. The '214 patent is unenforceable due to Plaintiffs' unclean hands.

12. The '214 patent is unenforceable as a result of inequitable conduct during prosecution before the PTO, as more particularly explained and alleged below.

13. The '214 patent is directed to dexmedetomidine, the *d*-enantiomer of medetomidine, which is an α_2-adrenergic receptor agonist. The '214 patent alleges that the *d*-enantiomer possesses highly enhanced α_2-selectivity and potency compared to the racemic mixture of medetomidine, which contains equal amounts of both the *d*-enantiomer and *l*-enantiomer. ('214 patent col. 2 ll.20-30.)

14. The originally filed claims of the '214 patent application were directed to, *inter alia*, the enantiomers of medetomidine and methods for separating them.

15. In an Office Action mailed March 17, 1989, the PTO rejected several of these claims as obvious in view of the prior art. The Examiner reasoned that it would have been obvious to separate racemic medetomidine into its enantiomers because it was known in the art that one enantiomer is typically more active than the other.

16. In their Amendment and Remarks filed September 18, 1989, the Applicants for the ’214 patent canceled claims directed to the *l*-enantiomer and the method for separating the enantiomers. To overcome the obviousness rejection and obtain allowance of the remaining claims directed to the *d*-enantiomer of medetomidine (*i.e.*, dexmedetomidine), the Applicants relied on data presented in Table 2 of the ’214 patent application. The Applicants emphasized the unexpected results allegedly achieved by the *d*-enantiomer and reflected in Table 2.

17. [REDACTED].

18. [REDACTED].

19. [REDACTED].

20. [REDACTED].

A. The Applicant’s Relied on Flawed Data in Table 2 of the ’214 Patent to Overcome the Examiner’s Obviousness Rejections

21. To overcome the Examiner’s March 17, 1989 obviousness rejection and obtain allowance of the claims directed to the *d*-enantiomer of medetomidine, the Applicants relied on data presented in Table 2 of the ’214 patent and emphasized the unexpected results allegedly achieved by the *d*-enantiomer.

TABLE 2

Compound	^{3}H-clonidine displacement IC_{50}, nM	^{3}H-prazosin displacement IC_{50}, nM	α_2/α_1-selectivity
d-enantiomer	1.2	55019	45849
l-enantiomer	46	189975	4129
medetomidine	3.3	16700	5060
detomidine	3.7	242	65
clonidine	6.4	6200	969

22. Table 2 of the ’214 patent purportedly shows, among other things, that the α_2/α_1 selectivity for the *d*-enantiomer (45849) is more than nine times greater than that for racemic

medetomidine (5060). Table 2 also purportedly shows that both the d- and l-enantiomers have an α1-agonist activity much less than that of racemic medetomidine.

23. The Applicants argued that the "selectivity data" in Table 2 of the '214 patent demonstrated the "surprising activity" of the *d*-enantiomer with respect to its α_2- α_1-selectivity ratio. The Applicants represented that the *d*-enantiomer had a selectivity for the α_2-adrenergic receptor over the α_1-adrenergic receptor that was "more than nine times that of the racemate." (September 18, 1989 Response to Office Action at 3 (emphasis added).) According to the Applicants, "[t]his advantageous effect is completely unexpected and could not be predicted." (*Id.* at 3-4.)

24. The Applicants also argued that "[g]iven the level of α_1-agonist activity of medetomidine one would expect at least one of the enantiomers to have a greater activity." (*Id.* at 3.) Relying on the data in Table 2, however, Applicants argued to the PTO that "[s]urprisingly. . . both enantiomers have an α_1-agonist activity which is much less than that of medetomidine". (*Id.*)

25. The PTO subsequently issued a Notice of Allowance and allowed the pending claims in the '214 patent application. The record shows that in allowing the pending claims and granting the patent, the PTO relied on the data in Table 2 of the '214 patent, the Applicants' representations regarding the α_2- α_1-selectivity ratio of dexmedetomidine, and the Applicants' representations regarding the α_1-agonist activity of the enantiomers as compared to racemic medetomidine.

B. [REDACTED].

26. [REDACTED].

27. [REDACTED].

28. [REDACTED].

29. [REDACTED].

30. As an initial matter, the data in Table 2 purportedly demonstrate synergy between the *d*- and *l*-enantiomers when binding to the α_1-adrenergic receptor. According to the data in the center column of Table 2, the IC_{50} of the *l*-enantiomer for the α_1-adrenergic receptor is 10-fold that of racemic medetomidine, and the IC_{50} of the *d*-enantiomer is 3.3 fold that of racemic medetomidine, suggesting synergistic binding by both enantiomers at separate sites on the α_1-adrenergic receptor.

TABLE 2

Compound	^{3}H-clonidine displacement IC_{50}, nM	^{3}H-prazosin displacement IC_{50}, nM	α_2/α_1-selectivity
d-enantiomer	1.2	55019	45849
l-enantiomer	46	189975	4129
medetomidine	3.3	16700	5060
detomidine	3.7	242	65
clonidine	6.4	6200	969

However, such a conclusion was contrary to the accepted model and understanding of α_1-adrenergic receptor activation at that time (and now), which contemplated only a single binding site. This clear and obvious disconnect between the experimental data and the scientific understanding of the α_1-adrenergic receptor would have caused one skilled in the art to doubt the validity and reliability of the data in Table 2, and to avoid drawing conclusions from such questionable data. Instead, however, Applicants affirmatively relied on that data and the selectivity ratios derived therefrom in alleging unexpected results to obtain allowance of the '214 patent.

31. Moreover, the data in Table 2 was inconsistent with the data in Tables 1, 3 and 4 of the '214 patent application. The data in Tables 1, 3 and 4 demonstrated that you would need roughly twice as much medetomidine as dexmedetomidine to get the same pharmacological

effect. This would have caused one skilled in the art to doubt the validity and reliability of the data in Table 2, and to avoid relying on the data to draw conclusions. Instead, however, the Applicants affirmatively relied on that data in alleging unexpected results to obtain allowance of the '214 patent.

32. Further, by 1988 the Applicants, including at least Dr. Virtanen, had concrete evidence that the Table 2 data submitted to the PTO was flawed and unreliable. In that year, work by Dr. Virtanen produced a drastically different selectivity ratio for medetomidine of 1620 rather than the 5060 reported in Table 2 of the '214 patent. *See* Virtanen, R. *et al*., Eur. J. Pharmac. 150:9-14 (1988) ("Virtanen 1988 Report"). The Virtanen 1988 Report was submitted and accepted for publication prior to the filing date of the '214 patent application with the PTO.

33. Dr. Virtanen also knew by 1988 that the data in Table 2 was obtained using a receptor binding assay whose shortcomings undermined the accuracy of the selectivity data. Dr. Virtanen's 1988 Report employed a superior receptor binding assay that was substantially improved in several respects, including changes to the method by which nonspecific binding was defined, the amount of radioligand used, buffer pH levels, specific amounts of tissue used, and assay wash protocols.

34. [REDACTED].

C. [REDACTED].

35. [REDACTED].

36. [REDACTED].

37. [REDACTED].

38. [REDACTED].

39. [REDACTED].

40. [REDACTED].

41. [REDACTED].

42. [REDACTED].

D. [REDACTED].

43. [REDACTED].

44. [REDACTED].

45. [REDACTED].

46. [REDACTED].

47. [REDACTED].

48. [REDACTED]. Dr. Virtanen and Dr. Savola were frequent co-authors of articles, writing at least three articles together relating to medetomidine or dexmedetomidine between 1986 and 1991, *i.e.*, the very subject matter of the '214 patent [REDACTED].

49. [REDACTED]. Dr. Virtanen and Dr. Savola were collaborating together on an article [REDACTED]—*Characterization of the selectivity, specificity and potency of medetomidine as an α2-adrenoceptor agonist*, European Journal of Pharmacology, 150 (1988) ("Virtanen/Savola 1988 Article"). [REDACTED].

50. [REDACTED].

51. [REDACTED].

52. [REDACTED].

53. [REDACTED].

54. [REDACTED].

55. [REDACTED].

56. [REDACTED].

57. [REDACTED].

58. [REDACTED].

59. [REDACTED].in 1990, Dr. Virtanen and Dr. Savola wrote an article published in the European Journal of Pharmacology entitled "Central α_2-adrenoceptors are highly stereoselective for dexmedetomidine, the dextro enantiomer of medetomidine." Eur. J. Pharm., 195 (1991) 193-199 ("Virtanen/Savola 1991"). This article was received in August 1990, revised in December 1990, and accepted in January 1991.

60. The Virtanen/Savola 1991 Article reported that "Medetomidine . . . is one of the most selective and potent agonists of α2-adrenoreceptors known," and further that "[t]he racemic medetomidine was slightly less potent than dexmedetomidine." This conclusion is contrary to Table 2 of the '214 patent and the arguments made in support of its patentability [REDACTED].

61. Dr. Virtanen was thus well aware of the known potency and selectivity of medetomidine, that medetomidine is only "slightly less potent than dexmedetomidine" against the α_2-adrenoreceptor, and that the selectivity ratios of medetomidine and dexmedetomidine were very similar.

62. In light of this article, [REDACTED]. Dr. Virtanen must have known that the wildly different α_1 data and selectivity ratios for medetomidine and dexmedetomidine reported in the '214 patent were inaccurate [REDACTED] long before issuance of the '214 patent.

63. [REDACTED].

64. [REDACTED].

E. [REDACTED].

65. [REDACTED].

66. As a co-inventor, Dr. Virtanen signed an Inventor's Declaration stating that he would disclose all information known to him to be material to patentability, and had an ongoing duty to disclose material information to the PTO throughout the entire prosecution of the '214 patent.

67. [REDACTED].

68. [REDACTED].

69. [REDACTED].

70. [REDACTED].

71. [REDACTED].

72. [REDACTED].

73. [REDACTED].

74. [REDACTED].

75. [REDACTED].

76. [REDACTED].

77. [REDACTED].

78. [REDACTED].

79. [REDACTED].

80. Dr. Virtanen's inequitable conduct was committed as part of a successful attempt to convince the Examiner of unexpected results achieved by the *d* enantiomer of medetomidine. Because the "*d* enantiomer" is a limitation recited in every issued claim of the '214 patent, every claim of the '214 patent was tainted by Dr. Virtanen's nondisclosure and misrepresentation.

81. The nondisclosure and misrepresentation described above was a breach of the duty of candor owed to the PTO, and constitutes inequitable conduct that renders all claims of the ’214 patent unenforceable.

82. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding the enforceability of the ’214 patent, and a judicial declaration of unenforceability is necessary and appropriate at this time.

FOURTH COUNTERCLAIM

(Declaratory Judgment of Noninfringement of the ’867 Patent)

83. Sandoz Canada hereby incorporates by reference each and every allegation set forth in paragraphs 1 through 63 of its Answer, 1 through 10 of its Affirmative Defenses, and 1 through 82 of these Counterclaims above.

84. Sandoz Canada and its Dexmedetomidine Hydrochloride Injection 100 mcg base/ml product (the “Sandoz product”) do not infringe the ’867 patent, directly or indirectly, either literally or by the doctrine of equivalents.

85. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding whether Sandoz Canada infringes the ’867 patent, and a judicial declaration of noninfringement is necessary and appropriate at this time.

FIFTH COUNTERCLAIM

(Declaratory Judgment of Invalidity of the ’867 Patent)

86. Sandoz Canada hereby incorporates by reference each and every allegation set forth in Paragraphs 1 through 63 of the Answer, 1 through 10 of the Affirmative Defenses, and 1 through 85 of these Counterclaims above.

87. The ’867 patent, and each claim thereof, is invalid for failing to comply with the requirements of the patent laws of the United States, particularly with regard to one or more of the requirements specified in Sections 101, 102, 103, and/or 112 of Title 35 of the United States Code.

88. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding the validity of the ’867 patent, and a judicial declaration of invalidity is necessary and appropriate at this time.

SIXTH COUNTERCLAIM

(Declaratory Judgment of Unenforceability of the ’867 Patent)

89. Sandoz Canada hereby incorporates by reference each and every allegation set forth in Paragraphs 1 through 63 of the Answer, 1 through 10 of the Affirmative Defenses, and 1 through 88 of these Counterclaims above.

90. The ’867 patent is unenforceable due to Plaintiffs’ unclean hands.

91. The ’867 patent is unenforceable as a result of inequitable conduct during prosecution before the PTO, as more particularly explained and alleged below.

92. The ’867 patent is directed to a method of sedating a patient in an intensive care unit by the administration of dexmedetomidine (the *d* enantiomer of medetomidine), wherein the patient remains arousable and oriented.

93. In 1993, five years prior to the ’867 patent filing date, a co-inventor named Riku Aantaa co-authored a scientific literature review comparing dexmedetomidine to clonidine, and concluded that the two compounds were equivalent. *See* Aantaa, R. and Scheinin, M., Acta Anesth. Scand. 37: 433-48 (1993) (“the Aantaa review”). The Aantaa review states at page 437 that “[t]he pharmacological actions of dexmedetomidine . . . closely resemble those of

clonidine." The Aantaa review also cites at page 435 various publications similarly concluding that the two drugs acted at the same site of action on their target receptor, and likewise states at Page 442 that the effects of dexmedetomidine "closely resemble those induced by clonidine."

94. None of these statements equating dexmedetomidine and clonidine were ever disclosed to the PTO during prosecution, even though the Aantaa review was published five years prior to the filing date of the '867 patent.

95. The Applicants, including Aantaa, instead adopted the exact opposite position during prosecution of the '867 patent, asserting that dexmedetomidine was unique and unlike other sedatives. Specifically, the '867 patent states that the applicants "have surprisingly discovered" that dexmedetomidine is an ideal agent for sedation and patient comfort, and that the "quality of sedation" is "unique" because patients sedated by dexmedetomidine remained "arousable and oriented" thus making their treatment easier. '867 patent, col. 4 ll.30-55.

96. The Applicants relied on this characterization during prosecution to demonstrate unexpected results in responding to an obviousness rejection in an August 9, 2002 submission to the PTO, noting that dexmedetomidine "produces an unexpected quality of sedation not achieved by other ICU sedatives" because "[p]atients are asleep but easily arousable and well-oriented . . . ." Later during examination, the Applicants amended the independent claims to specifically recite the limitation "wherein the patient remains arousable and orientated" and also continued to assert unexpected results for dexmedetomidine. The obviousness rejections were subsequently withdrawn and the application issued as the '867 patent.

97. In addition, Aantaa plainly knew of, but failed to disclose, an article entitled Talke, P. et al. "Effects of Perioperative Dexmedetomidine Infusion in Patients Undergoing Vascular Surgery," Anesthesiology 1995, 82, 620-633 (Talke 1995). The goal of the Talke study

was to evaluate the safety of dexmedetomidine in vascular surgery patients and thus, the study focused on the hemodynamic effects of dexmedetomidine infusion during and after surgery in a patient population at high risk for coronary artery disease. Aantaa, in articles published in 1997 – before the filing of the '867 patent – and 2006, cited Talke 1995 for its evaluation of dexmedetomidine and its comparison to clonidine.

98. Talke 1995 was highly material to the prosecution of the application for the '867 patent. Talke 1995 describes how patients were administered an i.v. infusion of dexmedetomidine beginning prior to surgery, and continuing through the intraoperative period and for 48 hours postoperatively. The study noted that after the initial infusion, patients in the medium and high dose groups "fell asleep but were easily arousable", and contained specific information about formulations and dosages that would have been material to the claims.

99. Aantaa signed an Inventor's Declaration stating that he would disclose all information known to him to be material to patentability. As the author of his own prior literature review, Aantaa was aware that his prior work directly refuted the positions being taken during prosecution, and as the author of publications citing Talke 1995, he likewise knew or should have known that Talke 1995 was material to his claims.

100. As a co-inventor, Aantaa had an ongoing duty to disclose material information to the PTO throughout prosecution of the '867 patent. However, he never cited, disclosed, or otherwise called the Examiner's attention to his own prior contrary statements comparing and equating dexmedetomidine and clonidine, nor the evidence from Talke 1995 concerning the character of dexmedetomidine sedation, mode of administration, and target concentrations and dosages. The Aantaa review and Talke 1995 were not cumulative to information already of record, and would have refuted or been inconsistent with the Applicants' position that

dexmedetomidine had achieved unique and unexpected results as a sedative. A reasonable examiner would have considered the prior contrary statements of a co-inventor important in deciding whether to allow the ’867 patent.

101. Despite the relevance and materiality of these references, Aantaa intentionally failed to disclose and withheld from the PTO these publications because that information would have undermined the patentability of the claimed invention. A deliberate intent to deceive may be inferred from these facts.

102. Withholding the prior inconsistent statements in Talke 1995 and the Aantaa review and relying on inaccurate characterizations regarding the unique and unexpected activity of dexmedetomidine was also a misrepresentation intended to deceive the PTO and obtain allowance of the ’867 patent.

103. There is no credible good-faith explanation based on mistake, inadvertence, or otherwise for the nondisclosure of the Aantaa review, whose nondisclosure instead reflected an intentional effort to deceive the PTO.

104. Because each claim recites the limitation “arousable and orientated,” and those attributes were relied upon in establishing unexpected results during prosecution, the nondisclosure of Talke 1995 and the Aantaa review tainted the issuance of every claim in the ’867 patent.

105. By intentionally withholding and misrepresenting material information and relying on that deception to obtain allowance of the ’867 patent in the manner described above, the Applicants, including at least Aantaa, breached the duty of candor owed to the PTO and committed inequitable conduct that renders all claims of the ’867 patent unenforceable.

106. Sandoz Canada reserves the right to further supplement or amend these allegations as more information becomes available through discovery.

107. There exists an actual controversy between Sandoz Canada and Plaintiffs regarding the enforceability of the '867 patent, and a judicial declaration of unenforceability is necessary and appropriate at this time.

PRAYER FOR RELIEF

WHEREFORE, Sandoz Canada asks this Court to enter judgment in its favor and grant the following relief:

1. Dismissing with prejudice the entirety of Plaintiffs' Amended Complaint;
2. Dismissing all remedies and relief sought by Plaintiffs in the Amended Complaint;
3. Declaring that Sandoz Canada has not infringed, and is not infringing, any patent at issue in this case, including the '214 and '867 patents;
4. Declaring that the patents at issue in this case, including the '214 and '867 patents, are invalid, unenforceable, and void in law;
5. Finding this to be an exceptional case and awarding Sandoz Canada its costs, attorneys' fees, and expenses pursuant to 35 U.S.C. § 285; and
6. Granting such other and further relief as the Court may deem just and proper.

Dated: January 18, 2011

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CERTIFICATE OF SERVICE

I hereby certify that on January 18, 2011, I served opposing counsel by e-mail and first class U.S. mail, and I electronically filed **SANDOZ CANADA INC.'S FIRST AMENDED ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' AMENDED COMPLAINT** with the Clerk of Court using the CM/ECF system which will also send notification of such filing to the following:

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I hereby certify that on January 18, 2011, I served opposing counsel by e-mail and first class U.S. mail, a copy of **SANDOZ CANADA INC.'S FIRST AMENDED ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' AMENDED COMPLAINT** to the following:

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